

US009999624B2

(12) United States Patent

May et al.

(10) Patent No.: US 9,999,624 B2

(45) **Date of Patent:** *Jun. 19, 2018

(54) COMBINATION ALZHEIMER THERAPY USING ANTI-N3PGLU ABETA ANTIBODIES + A BACE INHIBITOR

(71) Applicant: Eli Lilly and Company, Indianapolis, IN (US)

(72) Inventors: Patrick Cornelious May, Carmel, IN (US); Dustin James Mergott,

Zionsville, IN (US)

(73) Assignee: Eli Lilly and Company, Indianapolis,

IN (US)

(*) Notice: Subject to any disclaimer, the term of this

patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days. days.

This patent is subject to a terminal dis-

claimer.

(21) Appl. No.: 15/503,027

(22) PCT Filed: Sep. 8, 2015

(86) PCT No.: PCT/US2015/048807

§ 371 (c)(1),

(2) Date: Feb. 10, 2017

(87) PCT Pub. No.: **WO2016/043997**

PCT Pub. Date: Mar. 24, 2016

(65) Prior Publication Data

US 2017/0224702 A1 Aug. 10, 2017

Related U.S. Application Data

- (60) Provisional application No. 62/050,967, filed on Sep. 16, 2014.
- (51) Int. Cl.

 A61K 39/395 (2006.01)

 A61K 31/542 (2006.01)

 C07K 16/18 (2006.01)

 C07D 513/04 (2006.01)

 A61K 45/06 (2006.01)

 A61K 39/00 (2006.01)

(52) U.S. Cl.

CPC A61K 31/542 (2013.01); A61K 39/3955 (2013.01); A61K 45/06 (2013.01); C07D 513/04 (2013.01); C07K 16/18 (2013.01); A61K 2039/505 (2013.01); C07K 2317/24 (2013.01)

(58) Field of Classification Search

CPC A61K 31/542; A61K 39/3955; A61K 2039/505; A61K 45/06; C07K 16/18; C07D 513/04

See application file for complete search history.

(56) References Cited

U.S. PATENT DOCUMENTS

8,158,620	B2	4/2012	Suzuki et al.
8,278,334	B2	10/2012	Cumming et al.
8,338,407	B2	12/2012	Hall et al.
8,592,408	B2	11/2013	Hall et al.
8,841,293	B1	9/2014	Green et al.
8,940,734	B2	1/2015	Hall et al.
8,961,972	B2	2/2015	Lu et al.
8,987,254	B2	3/2015	Green et al.
2013/0142806	A1*	6/2013	Lu C07K 16/18
			424/142.1
2014/0275044	A1*	9/2014	Green A61K 31/542
			514/224.2

OTHER PUBLICATIONS

Jacobsen, et al., "Combined Treatment with a Bace Inhibitor and Anti-A1 Antibody Gantenerumab Enhances Amyloid Reduction in App Mice", Journal of Neuroscience 34(35) (2014) pp11621-11630. May, et al., "Robust Central Reduction of Amyloid- in Humans with an Orally Available, Non-Peptidic -Secretase Inhibitor", Journal of Neuroscience 31(46) (2011) pp16507-16516.

Demattos, et al., "Combination Therapy with a Plaque Specific Ao Antibody and Bace Inhibitor Results in Dramatic Plaque Lowering in Aged Pdapp Transgenic Mice", Jul. 16, 2014.

Alzforum, "Anti-Amyloid Therapies Combine Forces to Knock Out Plaques", Jul. 25, 2014.

* cited by examiner

Primary Examiner — Kimberly Ballard (74) Attorney, Agent, or Firm — Nelsen L. Lentz

(57) ABSTRACT

The present invention provides a method of treating a cognitive or neurodegenerative disease, comprising administering to a patient in need of such treatment an effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof; in combination with an effective amount of an anti-N3pGlu Abeta monoclonal antibody.

15 Claims, No Drawings